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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/677,733	10/01/2003	Kevin H. Gardner	UTSD:1510	4887

23379 7590 02/21/2006

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EXAMINER
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NASHED, NASHAAT T

ART UNIT	PAPER NUMBER
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1656

DATE MAILED: 02/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/677,733	GARDNER ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Nashaat T. Nashed, Ph. D.	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE <sup>3</sup>~~1~~ MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 01 October 2003.
- 2a) ☐ This action is **FINAL**.      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1 and 2 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1 and 2 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

Art Unit: 1656

The application has been amended as requested in the communication filed February 9, 2004. Accordingly, claims 1 and 2 have been amended.

Claims 1 and 2 are pending and under consideration.

The abstract of the disclosure is objected to because contains more than one paragraph. Correction is required. See MPEP § 608.01(b).

Claims 1 and 2 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1 and 2 are directed to a method of detecting the binding of a ligand or identifying a ligand for any PAS domain (claim 1) of any protein having any activity or any PAS domain of any PAS kinase (claim 2) from any biological source by NMR. While there are less than a handful of PAS domains known in the prior art which are described in the specification, PAS domains exhibit relatively poor sequence identity among members of the family and are difficult to identify, see Amezcua *et al.* at page 1349, last paragraph (Structure 2002, Vol. 10, pages 1349-1361). Through its reference to the parent applications, the instant specification, however, only provides a single representative species from the human PAS kinase of SEQ ID NO: 2 in which residues 131-237 are identified as the PAS domain of the PAS kinase encompassed by the claims. There is no disclosure of any particular structure to function/activity relationship in the single disclosed species of the PAS domain of PAS kinase or for that matter any PAS domain. The specification also fails to describe additional representative species of these PAS domains or PAS Kinases by any identifying structural characteristics or properties, for which no predictability of structure is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1 and 2 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following are the reasons for the rejections:

- (a) The acronym "PAS domain" is not defined by the specification or the claim, and one of ordinary skill in the art would not know the metes and

Art Unit: 1656

bound of the phrase. Amezcue *et al.* (Structure 2002, Vol. 10, pages 1349-1361) teach that PAS domain exhibit relatively poor sequence identity among members of this family of proteins, see page 1349, last paragraph. Thus, a clear definition of the PAS domain is not readily apparent either in the prior art or the specification.

- (b) The phrase "foreign ligand" in claim renders the claim indefinite because the resulting claim does not set forth the metes and bound of the claimed invention. The phrase is not defined by the claim or the specification and one of ordinary skill in the art would not know what a foreign ligand is. For examination purposes only, the phrase is assumed to mean "ligand".
- (c) The clause "that has no NMR-apparent a priori formed ligand cavity" in claim 1 renders the claim indefinite and confusing. The phrase appears to mean that atoms of the amino acid residues involved in binding the ligand have no NMR signals in any NMR experiment including  $^1\text{H}$ ,  $^{13}\text{C}$  and  $^{15}\text{N}$  in a single dimension or multidimensional NMR experiment under any condition, which is not possible.
- (d) The phrase "to infer the presence of the ligand specifically bound" in claim 1 renders the claim indefinite because the resulting claim does not set forth the metes and bound of the claimed invention. The mere comparison of two NMR spectra by itself is not sufficient to infer specificity of a bound ligand. It is the observation of changes in the chemical shifts and ordered structure in otherwise disordered region that infer the specificity of the ligand.
- (e) The phrase "PAS kinase PAS A" in claim 2 renders the claim indefinite and confusing. For examination purposes only, the phrase is assumed to mean the PAS A domain of PAS kinase.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fesik *et al.* (WO 97/18471) in view of any one of U. S. patents 5,843,683 (Edery *et al.*); 6,291,429 (Takahashi *et al.*); 6,436,654 (Berkenstam *et al.*).

Fesik *et al.* teach method of identifying compounds that binds proteins using NMR methods, which include comparing the NMR of  $^1\text{H}/^{15}\text{N}$  correlation spectra of  $^{15}\text{N}$  labeled protein in the presence and absence of a potential compound that binds to said protein, see abstract and page 7, lines 29-32. They motivate one of ordinary skill in the art to use their method as they teach the many advantages of using their method, see page 8, line 8 to the end of the page. Also, they teach the application of their method to several proteins, see examples 1-2 and 4. Thus, the method is applicable to any protein of interest. Fesik *et al.* do not teach the application of their method to identify compound that bind or interact with PAS domain or proteins.

Edery *et al.* teach that abnormalities in PAS domain protein function may cause certain conditions or diseases in human, such as human behaviour disorders and epithelial tissue cancer, see column 1, lines 41-55. Also, they teach that xenobiotics such the aryl hydrocarbon or dioxin complex (AH) with receptor containing PAS domain activates the metabolism of the xenobiotics in the liver and lungs of mammals, but the activation process produces gene products which are able to convert the xenobiotic to carcinogens, see column 2, lines 22-40. Thus, it appears that compounds that modulate the activity of the PAS domain would be useful in the prevention and treatment of disease, see column 3, lines 47-56.

Takahaski *et al.* teach the human and mouse genes and polypeptides component of the circadian clock (the clock polypeptide), which are member of the basic helix-loop-helix-PAS domain family of proteins, see column 7, lines 53-65. The polypeptide is thought to be involved in many regulatory functions in human, see column 16, line 8 through column 21, line 27. Also, Takahaski *et al.* teach that modulator of the clock polypeptide can be used for the identification of drugs for the treatment circadian rhythm dysfunctions, see column 9, lines 13-27.

Berkenstam *et al.* teach the various domains encompassed in human HIF-1 $\alpha$  including PAS-B residues 178-390 of the human protein and its function, see column 7, last paragraph and column 8, lines 31-37 and column 11, lines 11-62. Also, they teach compounds that modulate the activity of various domains are potentially useful in the regulation of target genes normally associated with HIF-1 $\alpha$  such as genes involved in angiogenesis, erythropoiesis, and glycolysis.

Each of Edery *et al.*, Takahaski *et al.* and Berkenstam *et al.* provide one of ordinary skill in the art with motivation to identify modulator of the PAS domains in various protein as they teach modulator of the PAS domain are potential drugs to prevent and treat serious diseases. Fesik *et al.* provide one of ordinary skill in the art with motivation to use their method to identify ligands for the PAS domains as they teach an easy method amenable to automation for identification of modulator of protein activity. Thus, it would have been obvious to one of ordinary skill in the art to use the method taught by Fesik *et al.* to identify potential compound that modulate the activity of the PAS domain protein. Thus, the claimed invention was within the ordinary skill in the

Art Unit: 1656

art to make and use at the time was made and was as a whole, clearly *prima facie* obvious.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1 and 2 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 9, 10, and 12 of U.S. Patent No. 6,319,679 ('679). Although the conflicting claims are not identical, they are not patentably distinct from each other. Claims 9 and 10 are directed to a method of detecting polypeptide-ligand binding by any method, wherein one of the polypeptide is residues 131-237 of SEQ ID NO: 2 corresponding to the PAS A domain of the PAS kinase of SEQ ID NO: 2. Claim 12 further limits claim 9 to the method of detection of the binding by NMR.

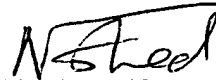
No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nashaat T. Nashed, Ph. D. whose telephone number is 571-272-0934. The examiner can normally be reached on MTWTF.

Art Unit: 1656

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen M. Kerr can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Nashaat T. Nashed, Ph. D.  
Primary Examiner  
Art Unit 1656